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The invention concerns the use of a liquid preparation, which contains a lipophilic gas solved, for the Neuroprotektion and neuro regeneration.

It is well-known that a cerebrale hypoxia/Ischämie releases a pathophysiological cascade, which finally leads to diaphragm and cell destruction and to the death of nerve cells. It is generally discussed that with this cascade the activation of NMDA and not NMDA receptors plays an important role. If these receptors are stimulated by high Glutamat or Aspartat concentrations, come it to a intrazellulären accumulation of Na< +> - and Ca< ++> - Ions and finally to swelling the cells. At the end of this unwanted cascade then cell death stands. In the research one turned in particular to the so-called NMDA receptor antagonists as potential neuroprotektive medicaments/drugs. Thus studies proved that Ketamin in large doses gives a neuro deficit decrease can. The administration of a Bolus with a small dose did not furnish however the desired effects. It admits is also that hurt neurons have an improved survival rate and a axonales growth is observed if one for example rats with S (+) - Ketamin treats. The clinical employment from Ketamin becomes however frequently because of the considerable side effects (z. B. increased blood pressure) did not consider.

The available invention is the basis the problem to make a preparation available some neuroprotektive and/or. neuroregenerativ effect, but not the side effects of Ketamin shows.

This problem is repaired by an aqueous solution, which contains solved a lipophilic gas. By lipophilic gas a molecule or a connection gaseous with standard conditions (atmospheric pressure, 20 DEG C) is understood here, which has a certain fat-solubleness. Expression for this is for example an oil/gas coefficient of > about 0.05 (krypton, 0,5; Argon, 0,15; Laughing gas, 1,4; Xenon, 1.9). Usually an oil is used such as n-Octanol for the measurement of this coefficient. One knows the lipophilic character also over the so-called Ostwald solubility (S. Gerald L. Pollak et al. in J. Chem. one. Physical one. 90 (11), 1989, ?Solubility OF xenon in 45 Organic solvency Including of cycloalkane, Acids and Alkanals: Experiment and Theory ") seize. The Ostwald solubility for xenon with 25 DEG C amounts to for example in n-hexane 4,8. By lipophilically the invention available in the sense one can understand alternatively such a gas that an Ostwald solubility > about 1.0 in n-hexane with 25 DEG C exhibits. This lipophilic gas can be present in very small concentrations. In particular in case of of xenon as lipophilic gas additionally a clear analgetische and anästhetische effect goes into action. It was now surprisingly stated that a intravasiv given, liquid preparation has a neuroprotektiven and neuroregenerativ effect.

The preparation according to invention is in particular intravenously given, whereby it is favourable to use a Bolus of 20-30 ml followed from a longer infusion to several days with a rate of 0,1-2 ml/min.

As case of model for a preparation according to invention an aqueous fat emulsion is regarded, which contains solved xenon with concentrations of 0,2-10 ml/ml the preparation (the indication of concentration refers here to the standard condition: 20 DEG C and atmospheric pressure). The xenon concentration in such a preparation depends on a multiplicity of factors, in particular the characteristics of the carrier. Usually one ?is loaded? the preparations according to invention to to the Sättigungsgrenze with xenon. With a 10%igen fat emulsion easily xenon concentrations can be achieved by 0,3-5 ml Xenon/ml preparation. These fat emulsions are at least in gas-tight locked containers sufficiently stable, so that that of xenon is not set free during usual storage times again as gas. In addition it showed up that these emulsions get over also usual heat sterilization with approximately 121 DEG C.

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The Lipidphase of the preparation, which takes up the gas, D. h. to solve and/or disperse can, essentially becomes by so-called. Fats in an educated manner, whereby it can essentially concern esters of langkettigen and mittellangkettigen fatty acids. Such fatty acids, satisfied or insatiated, contain 8 to 20 carbon atoms. In addition, besides omega-3 or omega-6-Fettsäuren can be used, which can contain carbon atoms up to 30. As veresterte fatty acids in particular vegetable oils offer themselves, like z. B. Cotton-seed oil, soy bean oil, thistle oil, Fischöl and such. Main part of these naturally occurring oils are the Triglyceride of the fatty acids. Preparations are of special importance, as so-called. Oil in water emulsions are present. The fat portion of the emulsion makes usually 5 to 30 Gew. - %, preferably 10 to 20 Gew. - % out. Beside the fat however usually an emulsifying agent is present, whereby Sojaphosphatide, gel or also Eiphosphatid worked. Such emulsions can be manufactured, as the oil in presence of the emulsifying agent, an surface-active means, in water, not mixable with water, is usually emulsified. Beside the water also different polar solvents, as for example ethanol, can be present Glycerin (propylene glycol, Hexylenglykol, polyethylene glycol, Glykolmonoether, with water of mixable esters, etc.). The noble gas can have been already brought in in a preceding Verfahrensstufe into the Lipidphase. In the simplest case offers itself however to load the finished emulsion with xenon. This can take place at different temperatures, for example at temperatures from 1 DEG C up to ambient temperature. Here it is occasionally helpful, the container, in which the emulsion is to subject with a pressure from for example to 8 atmospheres or over it.

Fat emulsions can according to invention be begun, as they are used with the intravenous nutrition. These fat emulsions essentially consist of a suitable fat basis (soy bean oil or sunflower core oil) and a good-compatible emulsifying agent (Phosphatide). Generally common fat emulsions are Intralipid TM, Intrafat TM, Lipofundin TM S and Liposyn TM. One knows more exact data to these fat emulsions G. Kleinberger and H. Pamperl, infusion therapy, 108-117 (1983) 3, take. The fat emulsions contain generally still of additives, which make the Osmolarität of of the aqueous phase, which surrounds the fat phase available in the form of Liposomen, for blood isotone. For this one can use Glycerin and/or Xylit. In addition it is frequently meaningful to add to the fat emulsion an antioxidant in order to prevent an oxidation of the insatiated fatty acids. For this in particular Vitamin E (DL Tocopherol) is suitable.

As Lipidphase, particularly favourably in particular with an oil in water emulsion, are so-called. Liposomen, itself from the Triglyceriden in addition, generally from so-called, mentioned above. Phospholipidmolekülen to form leave. This

Phospholipidmoleküle consists itself generally of a water-soluble part, which are formed by at least one group of phosphates, and a Lipidteil, from a fatty acid and/or. their ester derives.

In the US-A-5 334,381 in the detail one describes, how one can load Liposomen with gas. Spoken a device is completely generally filled with the Liposomen, D. h. with an oil in water emulsion, and then the device with the gas is pressurized therein. The temperature up to 1 DEG C can be lowered. Under pressure the gas dissolves gradually and arrives into the Liposomen. During a relaxation of the pressure it can come then to the training of small gas bubbles, which become in totally enclosed from the Liposomen however now. Thus it is practically possible to hold for example xenon gas or other gases under hyperable conditions in a fat emulsion. Also such preparations can be used according to invention, as long as it does not come to the training of a separate gaseous phase outside of the Liposomen and provided that occurs the pharmakologische effect desired.

The Lipide, which train the Liposomen, can be from natural or synthetic origin. Such materials are for example Cholesterol, Phosphatidylcholin, Phosphatidyl ethanolamin, Phosphatidylserin, Phosphatidylglycerin, Phosphatidylinositol, Sphingomyelin, Glycosphingolipide, Glucolipide, Glycolipide, etc. The surface of the Liposomen can be further with a polymer modified, for example with Polyethylenglycol.

A Lipidemulsion with a lipophilic gas can contain for example the following components:
5-20 g soy bean oil (10 g)
5-30 g Triglyceride of the C8-C10-Fettsäuren (for example Miglyol TM of the Hüls AG, Marl, Germany) (10 g)
0.5-2 g (1.2 g)
1-3 g Glycerol (2.5 g)
0-0.1 g (0.03 g) sodium oleate
Remainder water on 100 ml.

Such a preparation leaves itself easily as before described with 10-100 ml and over it the lipophilic gas be< DP N=6> load. For example one can proceed in such a way the fact that one dissolves first the lipophilic gas as for example xenon in a mixture from soy bean oil and Fettsäuretriglyceriden and then in the connection mixed with the aqueous phase (those the other components contains) and finally emulsifies the oil phase. Emulsion can be achieved among other things by means of a Homogenisators. Thus one keeps oil drops < size; 1 mu m (diameter), whereby the largest part of the lipophilic gas is then present in the oil drops (80-99%). Such an emulsion can be heat-sterilized easily and be stored at temperatures between 4 and 25 DEG C longer. It is favourable, if one works at the production of the preparation under an atmosphere of the lipophilic gas, for example xenon. In addition also purely aqueous solutions are applicable, whereby it offers itself, to add to these solutions substances which facilitate the dissolution of the Xenons in the preparation. Frequently straight have described the before, generally already admitted of restaurant anaesthetics this characteristic, since they exhibit a lipophilic remainder. Another example of a connection, those the dissolution of the lipophilic gas in particular in aqueous solutions promotes is among other things Vitamin E and/or. Tocopherole or complexing agents, as in the EP-A-0357163 described Cavitate or Clathrate, derived from it.